09-J3000-01

Original Effective Date: 06/15/18

Reviewed: 03/13/24

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Subject: Fosnetupitant-Palonosetron (Akynzeo) IV

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Chemotherapy-induced nausea and vomiting (CINV) can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy. The severity and incidence of CINV are affected by factors such as the selected agent and dose of chemotherapy, schedule and route of administration, and patient specific factors (e.g., age, sex, prior chemotherapy, history of alcohol use).

Fosnetupitant/palonosetron (Akynzeo IV) is a combined neurokinin-1(NK-1) receptor antagonist and serotonin (5HT3) receptor antagonist that was FDA approved in April 2018 for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. Fosnetupitant/palonosetron was approved based on bioequivalence of the intravenous formulation with the oral form of netupitant/palonosetron (Akynzeo capsules). Fosnetupitant is a prodrug that is converted to netupitant by metabolic hydrolysis.

National Comprehensive Cancer Network (NCCN) Guidelines for Antiemesis recommend NK1 receptor antagonist containing regimens (e.g., aprepitant, fosaprepitant, rolapitant, or netupitant) for acute and delayed emesis prevention in combination with dexamethasone and a serotonin antagonist with or without lorazepam, histamine-2 blockers, or proton pump inhibitors before intravenous antineoplastic therapy with high or moderate emetic risk. The use of an NK1 receptor antagonist is also recommended in combination with olanzapine, dexamethasone, and a serotonin antagonist for high-risk antineoplastic therapy or if emesis occurred during a previous cycle of antineoplastic therapy with a 3-drug regimen. NCCN specifically states that use of NK1 receptor antagonists are for the prevention of CINV, not treatment of CINV.

POSITION STATEMENT:

I. Fosnetupitant/palonosetron injection (Akynzeo IV®) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Use is for prevention of acute or delayed chemotherapy-induced nausea and vomiting associated with initial or repeat courses of chemotherapy
2. **ONE** of the following:
    a. Chemotherapy has a moderate or high emetogenic potential (Table 1)
    b. Chemotherapy has a low emetogenic potential (Table 1) and the member has an inadequate response to use of a serotonin antagonist (i.e., ondansetron, granisetron, or palonosetron) to prevent chemotherapy-induced nausea and vomiting†
3. Use is in combination with a corticosteroid (i.e., dexamethasone) * **OR** the member has a contraindication to corticosteroids
4. The member is not receiving an additional NK1 receptor antagonist (e.g., aprepitant, fosaprepitant, rolapitant, or netupitant/palonosetron)
5. The member is not receiving an additional serotonin antagonist for prevention of nausea and vomiting (e.g., palonosetron, subcutaneous granisetron)
6. The member had an inadequate response or intolerance to fosaprepitant used in combination with a serotonin antagonist (i.e., ondansetron, granisetron, or palonosetron) †
7. The dose does not exceed 235 mg fosnetupitant/0.25 mg palonosetron and is given prior to chemotherapy

Duration of approval: 1 year

*__Note__: Given with or without olanzapine, lorazepam, histamine-2 receptor blocker or proton pump inhibitor

†Step therapy requirement does not apply if the member was previously approved by Florida Blue or a prior health plan.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Fosnetupitant/palonosetron for injection is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. It has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide.

One reconstituted vial (235mg fosnetupitant/0.25mg palonosetron) is infused over 30 minutes starting 30 minutes prior to chemotherapy.

Dose Adjustments

Fosnetupitant/palonosetron for injection has not been studied in patients with severe renal impairment or severe hepatic impairment and use should be avoided.

Drug Availability

- 235 mg fosnetupitant/0.25 mg palonosetron in a single-dose vial as a solution or as a single-dose vial for reconstitution

PRECAUTIONS:

Contraindications – None

Precautions/Warnings

- **Hypersensitivity**– Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with palonosetron.
- **Serotonin syndrome—** Serotonin syndrome has occurred following the use of 5-HT3 receptor antagonists alone or in combination with other serotonergic drugs. Discontinue use and begin supportive treatment if serotonin syndrome develops.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1454	Injection, fosnetupitant 235 mg and palonosetron 0.25 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

R11.0	Nausea
R11.10 – R11.12	Vomiting, unspecified
R11.2	Nausea with vomiting, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T45.95XA	Adverse effect of unspecified primarily systemic and hematological agent, initial encounter
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

Acute chemotherapy-induced nausea and vomiting – nausea and/or vomiting that occurs within a few minutes to several hours after drug administration and commonly resolves within the first 24 hours.

Delayed chemotherapy-induced nausea and vomiting – nausea and/or vomiting that occurs 24 hours after drug administration.

RELATED GUIDELINES:

Aprepitant injectable therapy (Cinvanti®), 09-J2000-60

OTHER:

Table 1

Emetogenic Potential of Antineoplastic Agents		
	High emetic risk (>90% frequency of emesis)	**Moderate emetic risk (30-90% frequency of emesis)**
IV	AC combination (doxorubicin or epirubicin with cyclophosphamide) Carboplatin AUC ≥ 4 Carmustine (> 250 mg/m^2) Cisplatin Cyclophosphamide (> 1500 mg/m^2) Dacarbazine Doxorubicin (≥ 60 mg/m^2) Epirubicin (> 90 mg/ m^2) Fam-trastuzumab deruxtecan-nxki Ifosfamide (≥ 2 g/ m^2) Mechlorethamine Melphalan (≥ 140 mg/m^2) Sacituzumab govitecan-hziy Streptozocin	Aldesleukin (> 12-15 million IU/m^2) Amifostine (> 300 mg/m^2) Bendamustine Busulfan Carboplatin AUC < 4 Carmustine (≤ 250 mg/m^2) Clofarabine Cyclophosphamide (≤ 1500 mg/m^2) Cytarabine (> 200 mg/m^2) Dactinomycin Daunorubicin Dinutuximab Doxorubicin (< 60 mg/m^2) Dual-drug liposomal encapsulation of cytarabine and daunorubicin Epirubicin (≤ 90 mg/m^2) Idarubicin Ifosfamide (< 2g/m^2)

		Irinotecan Irinotecan (liposomal) Lurbinectedin Melphalan (< 140 mg/m^2) Methotrexate (≥ 250 mg/m^2) Mirvetuximab soravtansine-gynx Naxitamab-gqgk Oxaliplatin Romidepsin Temozolomide Trabectedin
IV	**Low emetic risk (10 – 30% frequency of emesis)**	
	Ado-trastuzumab emtansine Aldesleukin ≤ 12 million international units/m^2 Amifostine ≤ 300 mg/m^2 Amivantamab-vmjw Arsenic trioxide Axicabtagene ciloleucel Azacitidine Belinostat Brexucabtagene autoleucel Brentuximab vedotin Cabazitaxel Carfilzomib Ciltacabtagene autoleucel Copanlisib Cytarabine (low dose) 100 – 200 mg/m^2 Docetaxel Doxorubicin (liposomal) Enfortumab vedotin-ejfv Eribulin Etoposide 5-FU Floxuridine Gemcitabine Gemtuzumab ozogamicin Idecabtagene vicleucel Inotuzumab ozogamicin Isatuximab-irfc Ixabepilone Lisocabtagene maraleucel Loncastuximab tesirine-lpyl Methotrexate > 50 mg/m^2 - < 250 mg/m^2 Mitomycin	

	Mitomycin pyelocalyceal solution Mitoxantrone Mogamulizumab-kpkc Mosunetuzumab-axgb Necitumumab Omacetaxine Paclitaxel Paclitaxel-albumin Pemetrexed Pentostatin Polatuzumab vedotin-piig Pralatrexate Tafasitamab-cxix Tagraxofusp-erzs Talimogene laherparepvec Tebentafusp-tebn Thiotepa Tisagenlecleucel Tisotumab vedotin-tftv Topotecan Ziv-aflibercept

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/13/24.

GUIDELINE UPDATE INFORMATION:

06/15/18	New Medical Coverage Guideline.
10/01/18	Revision to guideline consisting of adding HCPCS code C9033.
01/01/19	Revision: HCPCS code updates. Added J1454, and removed C9033 and J3490.
05/15/19	Review and revision to guideline consisting of updating Table 1 and references.
01/01/20	Revision to guideline; consisting of updating the position statement.
05/01/20	Review and revision to guideline; consisting of updating Table 1 and references.
12/15/20	Review and revision to guideline; consisting of updating the position statement and references.
05/15/21	Review and revision to guideline; consisting of updating Table 1 and references.
05/15/22	Review and revision to guideline; consisting of updating Table 1, description, and references.
04/15/23	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.
04/15/24	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.